

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: BLAZAR, *et al.*

Application No.: 10/827,023

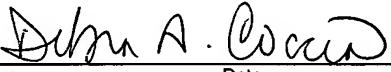
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Title: Regulatory T Cells and Their Use In Immunotherapy and Suppression of Autoimmune Responses

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Respectfully submitted,

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GROUP 1636

**U.S. PATENT DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if appropriate

**FOREIGN PATENT DOCUMENTS**

		Document Number	Date	Country	Class	Subclass	Translation Yes/No/Abstract

**OTHER DOCUMENT(S) (Including Author, Title, Date, Pertinent Pages, etc.)**

1.	Anasetti C, Martin PJ, Storb R, Appelbaum FR, Beatty PG, Calori E, Davis J, Doney K, Reichert T, Stewart P, <i>et al.</i> , "Prophylaxis of graft-versus-host disease by administration of the murine anti-IL-2 receptor antibody 2A3," <i>Bone Marrow Transplant</i> 7:375-381 (1991).
2.	Apostolou, I., Sarukhan, A., Klein, L., vonBoehmer, H., "Origin of regulatory T cells with known specificity for antigen," <i>Nat Immunol</i> 3(8):756-763 (2002).
3.	Asano M, Toda M, Sakaguchi N, Sakaguchi S, "Autoimmune disease as a consequence of developmental abnormality of a T cell subpopulation," <i>J. Exp. Med.</i> 184:387-396 (1996).
4.	Asseman, C., Mauze, S., Leach, M.W., Coffman, R.L., Powrie, F., "An essential role for interleukin 10 in the function of regulatory T cells that inhibit intestinal inflammation," <i>J Exp Med</i> 190(7):995-1004 (1999).
5.	Baecher-Allan C, Brown JA, Freeman GJ, Hafler DA, "CD4+CD25 high regulatory cells in human peripheral blood," <i>J. Immunol.</i> 167:1245-1253 (2001)
6.	Banchereau, J., Briere, F., Caux, C., Davoust, J., Lebecque, S., Liu, Y.J., Pulendran, B., Palucka, K., "Immunobiology of dendritic cells," <i>Annu Rev Immunol</i> 18:767-811 (2000).
7.	Belkaid, Y., Piccirillo, C.A., Mendez, S., Shevach, E.M., Sacks, D. L., "CD4+CD25+ regulatory T Cells control Leishmania major persistence and immunity," <i>Nature</i> 420(6915):502-507 (2002).
8.	Blaise D, Olive D, Hirn M, Viens P, Lafage M, Attal M, Stoppa AM, Gabert J, Gastaut JA, Camerlo J, <i>et al.</i> , "Prevention of acute GVHD by <i>in vivo</i> use of anti-interleukin-2 receptor monoclonal antibody (33B3.1): a feasibility trial in 15 patients," <i>Bone Marrow Transplant</i> 8:105-111 (1991).
9.	Bonomo A, Kehn PJ, Payer E, Rizzo L, Cheever AW, Shevach EM, "Pathogenesis of post-thymectomy autoimmunity. Role of syngeneic MLR- reactive T cells," <i>J. Immunol.</i> 154:6602-6611 (1995).
10.	Cahn JY, Bordigoni P, Tiberghien P, Milpied N, Brion A, Widjenes J, Lioure B, Michel G, Burdach S, Kolb HJ, <i>et al.</i> , "Treatment of acute graft-versus-host disease with methylprednisolone and cyclosporine with or without an anti-interleukin-2 receptor monoclonal antibody. A multicenter phase III study," <i>Transplantation</i> 60:939-942 (1995).
11.	Carpenter PA, Pavlovic S, Tso JY, Press OW, Gooley T, Yu XZ, Anasetti C, "Non-Fc receptor-binding humanized anti-CD3 antibodies induce apoptosis of activated human T cells," <i>J. Immunol.</i> 165:6205-6213 (2000).

12.	Cella, M., Salio, M., Sakakibara, Y., Langen, H., Julkunen, I., Lanzavecchia, A., "Maturation, activation, and protection of dendritic cells induced by double-stranded RNA," <i>J Exp Med</i> 189(5):821-829 (1999).
13.	Chai, J.G., Tsang, J.Y., Lechler, R., Simpson, E., Dyson, J., Scott, D., "CD4+CD25+ T Cells as immunoregulatory T cells in vitro," <i>Eur J Immunol</i> 32(8):2365-2375 (2002).
14.	Chatenoud L, Salomon B, Bluestone JA, "Suppressor T cells--they're back and critical for regulation of autoimmunity!" <i>Immunol. Rev.</i> 182:149-163 (2001)
15.	Chen, W., W. Jin, and S. M. Wahl, "Engagement of cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) induces transforming growth factor beta (TGF-beta) production by murine CD4(+) T cells," <i>J. Exp. Med.</i> 188:1849-1857 (1998).
16.	Cohen, J.L., Trenado, A., Vasey, D., Klatzmann, D., Salomon, B.L., "CD4(+)CD25(+) immunoregulatory T cells: new therapeutics for graft-versus-host disease," <i>J Exp Med</i> 196(3):401-406 (2002).
17.	Dieckmann D, Plottner H, Berchtold S, Berger T, Schuler G, "Ex vivo isolation and characterization of CD4(+)CD25(+) T cells with regulatory properties from human blood," <i>J. Exp. Med.</i> 193:1303-1310 (2001).
18.	Dye, E. S. and R. J. North, "T cell-mediated immunosuppression as an obstacle to adoptive immunotherapy of the P815 mastocytoma and its metastases," <i>J. Exp. Med.</i> 154:1033-1042 (1981).
19.	Edinger, M., Hoffmann, P., Ermann, J., Drago, K., Fathman, C.G., Strober, S., Negrin, R.S., "CD4+CD25+ regulatory T cells preserve graft-versus-tumor activity while inhibiting graft-versus-host disease after bone marrow transplantation," 9(9):1144-1150 (2003).
20.	Fukaura, H., S. C. Kent, M. J. Pietrusiewicz, S. J. Khouri, H. L. Weiner, and D. A. Hafler, "Induction of circulating myelin basic protein and proteolipid protein-specific transforming growth factor-beta1-secreting Th3 T cells by oral administration of myelin in multiple sclerosis patients," <i>J. Clin. Invest.</i> 98:70-77 (1996).
21.	Gallimore, A., Sakaguchi, S., "Regulation of tumour immunity by CD25+ T cells," <i>Immunology</i> 107(10):5-9 (2002).
22.	Gao Q, Rouse TM, Kazmerzak K, Field EH, "CD4+CD25+ cells regulate CD8 cell anergy in neonatal tolerant mice," <i>Transplantation</i> 68:1891-1897 (1999).
23.	Gavin, M., Rudensky, A., "Control of immune homeostasis by Naturally Arising Regulatory CD4+ T Cells," <i>Curr Opin Immunol</i> 15(6):690-696 (2003).
24.	Godfrey, W.R., Krampf, M.R., Taylor, P.A., Blazar, B.R., "Ex vivo depletion of alloreactive cells based on CFSE dye dilution, activation antigen selection, and dendritic cell stimulation," <i>Blood</i> 103:1158-1165 (February, 2004).
25.	Godfrey, W.R., Spoken, D., Ge, Y., Levine, B., June, C., Blazar, B.R., and Porter, S., "In vitro expanded human CD4+CD25+ T regulatory cells can markedly inhibit allogeneic dendritic cell stimulated MLR cultures," <i>Blood</i> 104(2):453-461 (15 July 2004).
26.	Greenfield, E. A., E. Howard, T. Paradis, K. Nguyen, F. Benazzo, P. McLean, P. Hollsberg, G. Davis, D. A. Hafler, A. H. Sharpe, G. J. Freeman, and V. K. Kuchroo, "B7.2 expressed by T cells does not induce CD28-mediated costimulatory activity but retains CTLA4 binding: implications for induction of antitumor immunity to T cell tumors," <i>J. Immunol.</i> 158:2025-2034 (1997).

27.	Groux H, O'Garra A, Bigler M, Rouleau M, Antonenko S, de Vries JE, Roncarolo MG, "A CD4+ T-cell subset inhibits antigen-specific T-cell responses and prevents colitis," <i>Nature</i> 389:737-42 (1997).
28.	Hall, B.M., Fava, L., Chen, J., Plain, K. M., Boyd, R.A., Spicer, S.T., Berger, M.F., "Anti-CD4 monoclonal antibody-induced tolerance to MHC-incompatible cardiac allografts maintained by CD4+ suppressor T cells that are not dependent upon IL-4," <i>161(10):5147-5146</i> (1998).
29.	Hansen, J. A., P. J. Martin, and R. C. Nowinski, "Monoclonal antibodies identifying a novel T-cell antigen and Ia antigens of human lymphocytes," <i>Immunogenetics</i> 10:247-260 (1980).
30.	Hara, M., C. I. Kingsley, M. Niimi, S. Read, S. E. Turvey, A. R. Bushell, P. J. Morris, F. Powrie, and K. J. Wood, "IL-10 is required for regulatory T cells to mediate tolerance to alloantigens <i>in vivo</i> ," <i>J. Immunol.</i> 166:3789-3796 (2001).
31.	Harris DT, Sakiestewa D, Lyons C, Kreitman RJ, Pastan I, "Prevention of graft-versus-host disease (GVHD) by elimination of recipient-reactive donor T cells with recombinant toxins that target the interleukin 2 (IL-2) receptor," <i>Bone Marrow Transplant</i> 23:137-144 (1999).
32.	Hoffmann, P., Ermann, J., Edinger, M., Fathman, C.B., Strober, S., "Donor-type CD4(+)CD25(+) regulatory T cells suppress lethal acute graft-versus-host disease after allogeneic bone marrow transplantation," <i>J Exp Med</i> 196(3):389-399 (2002).
33.	Jiang, S., Camara, N., Lombardi, G., Lechler, R.I., "Induction of allopeptide-specific human CD4+CD25+ regulatory T cells <i>ex vivo</i> ," <i>Blood</i> 102(6):2180-2186 (2003).
34.	Jones, S.C., Murphy, G.F., Korngold, R., "Post-hematopoietic cell transplantation control of graft-versus-host disease by donor CD425 T cells to allow an effective graft-versus-leukemia response," <i>Biol Blood Marrow Transplant</i> 9(4):243-256 (2003).
35.	Jonuleit H, Schmitt E, Kakirman H, Stassen M, Knop J, Enk AH, "Infectious tolerance: human CD25(+) regulatory T cells convey suppressor activity to conventional CD4(+) T helper cells," <i>J. Exp. Med.</i> 196:255-260 (2002)
36.	Jonuleit, H., E. Schmitt, M. Stassen, A. Tuettenberg, J. Knop, and A. H. Enk, "Identification and functional characterization of human CD4(+)CD25(+) T cells with regulatory properties isolated from peripheral blood," <i>J. Exp. Med.</i> 193:1285-1294 (2001).
37.	Kung, P., G. Goldstein, E. L. Reinherz, and S. F. Schlossman, "Monoclonal antibodies defining distinctive human T cell surface antigens," <i>Science</i> 206:347-349 (1979).
38.	Laport, G.G., Levine, B.I., Stadmauer, E.A., Schuster, S.J., Luger, S.M., Grupp, S., Bunin, N., Stroble, F.J., Cotte, J., Zheng, Z., Gregson, B., Rivers, P., Vonderheide, R.H., Liebowitz, D.N., Porter, D.L., June, C.H., "Adoptive transfer of costimulated T cells induces lymphocytosis in patients with relapsed/refractory non-Hodgkin lymphoma following CD34+ selected hematopoietic cell transplantation," <i>Blood</i> 102(6):2004-2013 (2003).
39.	Lenardo MJ, "Interleukin-2 programs mouse alpha beta T lymphocytes for apoptosis," <i>Nature</i> 353:858-861 (1991).
40.	Levine, B.L., Bernstein, W.B., Connors, M., Craighead, N., Lindsten, T., Thompson, C.B., June, C.H., "Effects of CD28 costimulation on long-term proliferation of CD4+ T cells in the absence of exogenous feeder cells," <i>J. Immunol.</i> 159(12): 5921-5930 (1997).

41.	Levings MK, Sangregorio R, Sartirana C, Moschin AL, Battaglia M, Orban PC, Roncarolo MG, "Human CD25+CD4+ T suppressor cell clones produce transforming growth factor beta, but not interleukin 10, and are distinct from type 1 T regulatory cells," <i>J. Exp. Med.</i> 196:1335-1346 (2002).
42.	Levings, M. K., Sangregorio, R., and Roncarolo, M.G., "Human cd25(+)cd4(+) t regulatory cells suppress naive and memory T cell proliferation and can be expanded in vitro without loss of function," <i>J. Exp. Med.</i> 193:1295-1302 (2001).
43.	Lin, C.H., Hunig, T., "Efficient expansion of regulatory T cells <i>in vitro</i> and <i>in vivo</i> with a CD28 superagonist," <i>Eur J. Immunol</i> 33(3):626-638 (2003).
44.	Lissy NA, Van Dyk LF, Becker-Hapak M, Vocero-Akbani A, Mendler JH, Dowdy SF, "TCR antigen-induced cell death occurs from a late G1 phase cell cycle check point," <i>Immunity</i> 8:57-65 (1998).
45.	Nakamura K, Kitani A, Strober W, "Cell contact-dependent immunosuppression by CD4(+)CD25(+) regulatory T cells is mediated by cell surface-bound transforming growth factor beta," <i>J. Exp. Med.</i> 194:629-644 (2001).
46.	Ng, W.F., Duggan, P.J., Ponchel, F., Matarese, G., Lombardi, G., Edwards, A.D., Isaacs, J.D., Lechler, R.I., "Human CD4(+)CD25(+) cells: a naturally occurring population of regulatory T cells," <i>Blood</i> 98(9):2736-2744 (2001).
47.	Ochsenbein, A. F., S. Sierro, B. Odermatt, M. Pericin, U. Karrer, J. Hermans, S. Hemmi, H. Hengartner, and R. M. Zinkernagel, "Roles of tumour localization, second signals and cross priming in cytotoxic T-cell induction," <i>Nature</i> 411:1058-1064 (2001).
48.	Onizuka S, Tawara I, Shimizu J, Sakaguchi S, Fujita T, Nakayama E, "Tumor rejection by <i>in vivo</i> administration of anti-CD25 (interleukin-2 receptor alpha) monoclonal antibody," <i>Cancer Res.</i> 59:3128-3133 (1999).
49.	Pasare, C., Medzhitov, R., "Toll pathway-dependent blockade of CD4+CD25+ T cell-mediated suppression by dendritic cells," <i>Science</i> (5609):1033-1036 (2003).
50.	Peng, L., Kjaergaard, J., Plautz, G.E., Awad, M., Drazba, J.A., Shu, S., Cohen, P.A., "Tumor-induced L-selectin high suppressor T cells mediate potent effector T cell blockade and cause failure of otherwise curative adoptive immunotherapy," <i>J. Immunol</i> 169(9): 4811-4821 (2002).
51.	Piccirillo CA, Shevach EM, "Cutting edge: control of CD8+ T cell activation by CD4+CD25+ immunoregulatory cells," <i>J. Immunol.</i> 167:1137-1140 (2001).
52.	Read S, Malmstrom V, Powrie F, "Cytotoxic T lymphocyte-associated antigen 4 plays an essential role in the function of CD25(+)CD4(+) regulatory cells that control intestinal inflammation," <i>J. Exp. Med.</i> 192:295-302 (2000).
53.	S. Sakaguchi, "Naturally arising CD4 regulatory T cells for immunologic self-tolerance and negative control of immune responses," <i>Annu Rev Immunol</i> (2004, published on-line November 17, 2003).
54.	Sakaguchi S, Sakaguchi N, Asano M, Itoh M, Toda M, "Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases." <i>J. Immunol.</i> 155:1151-1164 (1995).
55.	Sakaguchi, S., N. Sakaguchi, J. Shimizu, S. Yamazaki, T. Sakihama, M. Itoh, Y. Kuniyasu, T. Nomura, M. Toda, and T. Takahashi, "Immunologic tolerance maintained by CD25+ CD4+ regulatory T cells: their common role in controlling autoimmunity, tumor immunity, and transplantation tolerance," <i>Immunol. Rev.</i> 182:18-32 (2001).

	56.	Sallusto, F., Lanzavecchia, A., "Efficient presentation of soluble antigen by cultured human dendritic cells is maintained by granulocyte/macrophage colony-stimulating factor plus interleukin 4 and downregulated by tumor necrosis factor alpha," <i>J Exp Med</i> 179(4):1109-1118 (1994).
	57.	Salomon B, Lenschow DJ, Rhee L, Ashourian N, Singh B, Sharpe A, Bluestone JA, "CD28 costimulation is essential for the homeostasis of the CD4+CD25+ immunoregulatory T cells that control autoimmune diabetes," <i>Immunity</i> 12:431-440 (2000).
	58.	Shevach EM. "CD4+ CD25+ suppressor T cells: more questions than answers," <i>Nat. Rev. Immunol.</i> 2:389-400 (2002)
	59.	Shevach, E. M., "Certified professionals: CD4(+)CD25(+) suppressor T cells," <i>J. Exp. Med.</i> 193:F41-F46 (2001).
	60.	Shevach, E. M., "Regulatory T cells in autoimmunity," <i>Annu. Rev. Immunol.</i> 18:423-449 (2000).
	61.	Shevach, E.M., Mcugh, R.S., Piccirillo, C.A., Thornton, A.M., "Control of T-cell activation by CD4+CD25+ suppressor T cells," <i>Immunol Rev</i> 182:58-67 (2001).
	62.	Shimizu J, Yamazaki S, Sakaguchi S, "Induction of tumor immunity by removing CD25+CD4+ T cells: a common basis between tumor immunity and autoimmunity," <i>J. Immunol.</i> 163:5211-5218 (1999).
	63.	Spisek, R., Bretaudeau, L., Barbieux, I., Meflah, K., Gregoire, M., "Standardized generation of fully mature p70 IL-12 secreting monocyte-derived dendritic cells for clinical use," <i>Cancer Immunol Immunother</i> 50(8):417-421 (2001).
	64.	Staveley-O'Carroll, K., E. Sotomayor, J. Montgomery, I. Borrello, L. Hwang, S. Fein, D. Pardoll, and H. Levitsky, "Induction of antigen-specific T cell anergy: An early event in the course of tumor progression," <i>Proc. Natl. Acad. Sci. USA</i> 95:1178-1183 (1998).
	65.	Stephens, L. A., C. Mottet, D. Mason, and F. Powrie, "Human CD4(+)CD25(+) thymocytes and peripheral T cells have immune suppressive activity <i>in vitro</i> ," <i>Eur. J. Immunol.</i> 31:1247-1254 (2001).
	66.	Suri-Payer E, Amar AZ, Thornton AM, Shevach EM, "CD4+CD25+ T cells inhibit both the induction and effector function of autoreactive T cells and represent a unique lineage of immunoregulatory cells," <i>J. Immunol.</i> 160:1212-1218 (1998).
	67.	Suri-Payer E, Kehn PJ, Cheever AW, Shevach EM, "Pathogenesis of post-thymectomy autoimmune gastritis. Identification of anti-H/K adenosine triphosphatase-reactive T cells," <i>J. Immunol.</i> 157:1799-1805 (1996).
	68.	Sutmuller, R. P., L. M. van Duivenvoorde, A. van Elsas, T. N. Schumacher, M. E. Wildenberg, J. P. Allison, R. E. Toes, R. Offringa, and C. J. Melief, "Synergism of cytotoxic T lymphocyte-associated antigen 4 blockade and depletion of CD25(+) regulatory T cells in antitumor therapy reveals alternative pathways for suppression of autoreactive cytotoxic T lymphocyte responses," <i>J. Exp. Med.</i> 194:823-832 (2001).
	69.	Suvas, S., Kumaraguru, U., Pack, C.D., Lee, S., Rouse, B.T., "CD4+CD25+ T Cells regulate virus-specific primary and memory CD8+ T cell responses," <i>J Exp Med</i> 198(6):889-901 (2003).
	70.	Taams, L. S., J. Smith, M. H. Rustin, M. Salmon, L. W. Poulter, and A. N. Akbar, "Human anergic/suppressive CD4(+)CD25(+) T cells: a highly differentiated and apoptosis-prone population," <i>Eur. J. Immunol.</i> 31:1122-1131 (2001).

	71.	Takahashi T, Kuniyasu Y, Toda M, Sakaguchi N, Itoh M, Iwata M, Shimizu J, Sakaguchi S, "Immunologic self-tolerance maintained by CD25+CD4+ naturally anergic and suppressive T cells: induction of autoimmune disease by breaking their anergic/suppressive state," <i>Int. Immunol.</i> 10:1969-1980 (1998).
	72.	Takahashi T, Tagami T, Yamazaki S, Uede T, Shimizu J, Sakaguchi N, Mak TW, Sakaguchi S, "Immunologic self-tolerance maintained by CD25(+)CD4(+) regulatory T cells constitutively expressing cytotoxic T lymphocyte-associated antigen 4," <i>J. Exp. Med.</i> 192:303-310 (2000).
	73.	Taylor PA, Noelle RJ, Blazar BR, "CD4(+)CD25(+) immune regulatory cells are required for induction of tolerance to alloantigen via costimulatory blockade," <i>J. Exp. Med.</i> 193:1311-1318 (2001).
	74.	Taylor, P.A., Lees, C.J., Blazar, B.R., "The infusion of <i>ex vivo</i> activated and expanded CD4(+)CD25(+) immune regulatory cells inhibits graft-versus-host disease lethality," <i>Blood</i> 99(10):3493-3499 (2002).
	75.	Thornton AM, Shevach EM, "CD4+CD25+ immunoregulatory T cells suppress polyclonal T cell activation <i>in vitro</i> by inhibiting interleukin 2 production," <i>J. Exp. Med.</i> 188:287-296 (1998).
	76.	Thornton AM, Shevach EM, "Suppressor effector function of CD4+CD25+ immunoregulatory T cells is antigen nonspecific," <i>J. Immunol.</i> 164:183-190 (2000).
	77.	Thornton, A.M., Piccarillo, C.A., Shevach, E.M., "Activation requirements for the induction of CD4+CD25+ T cell suppressor function," <i>Eur J Immunol</i> 34(2):366-376 (2004).
	78.	Thorstenson, K.M., Khoruts, A., "Generation of anergic and potentially immunoregulatory CD25+CD4 T cells <i>in vivo</i> after induction of peripheral tolerance with intravenous or oral antigen," <i>J Immunol</i> 167(1):188-195 (2001).
	79.	Trenado, A., Charlotte, F., Fisson, S., Yagello, M., Klatzmann, D., Salomon, B.L., Cohen, J.L., "Recipient-type specific CD4+CD25+ regulatory T cells favor immune reconstitution and control graft-versus-host disease while maintaining graft-versus-leukemia," <i>J Clin Invest</i> 112(11):1688-1696 (2003).
	80.	Vella AT, Dow S, Potter TA, Kappler J, Marrack P, "Cytokine-induced survival of activated T cells <i>in vitro</i> and <i>in vivo</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 95:3810-3815 (1998).
	81.	Walker, M.R., Kasprowicz, D.J., Gersuk, V.H., Benard, A., VanLandeghen, M., Buckner, J.H., Ziegler, S.F., "Induction of FoxP3 and acquisition of T regulatory activity by stimulated human CD4+CD25+ T cells," <i>J Clin Invest</i> 112(9):1437-1443 (2003).
	82.	Wesselborg S, Janssen O, Kabelitz D, "Induction of activation-driven death (apoptosis) in activated but not resting peripheral blood T cells," <i>J. Immunol.</i> 150:4338-4345 (1993).
	83.	Willerford DM, Chen J, Ferry JA, Davidson L, Ma A, Alt FW, "Interleukin-2 receptor alpha chain regulates the size and content of the peripheral lymphoid compartment," <i>Immunity</i> 3:521-530 (1995).
	84.	Woo, E. Y., C. S. Chu, T. J. Goletz, K. Schlienger, H. Yeh, G. Coukos, S. C. Rubin, L. R. Kaiser, and C. H. June, "Regulatory CD4(+)CD25(+) T cells in tumors from patients with early-stage non-small cell lung cancer and late-stage ovarian cancer," <i>Cancer Res.</i> 61:4766-4772 (2001).
	85.	Wood., K.J., Sakaguchi, S., "Regulatory T cells in transplantation tolerance," <i>Nat Rev Immunol</i> 3(3):199-210 (2003).
	86.	Yamagiwa S, Gray JD, Hashimoto S, Horwitz DA, "A role for TGF-beta in the generation and expansion of CD4+CD25+ regulatory T cells from human peripheral blood," <i>J. Immunol.</i> 166:7282-7289 (2001).

Examiner Signature:

Date Considered:

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